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Resting Electroencephalography Differences Between Eyes-Closed and Eyes-Open Conditions in Children with Subclinical Hypothyroidism

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What is already known on this topic?

- *There are concerns about the long-term effects of subclinical hypothyroidism (SH), especially in children in whom minor abnormalities may damage neurocognitive development. Neurocognitive function tests have shown that children with SH have poor performance in attention tests compared to the control group. Besides, neuro-electrical variances were detected via electrophysiological investigations.*

What this study adds on this topic?

- *The present study analyzes the resting brain electrical activity in children with subclinical hypothyroidism (SH). While moving from the eyes-closed (EC) state to the eyes-open (EO) state, visual information input starts. Visual input enhanced the functional innervation of the visual system, which activates the entire brain. Electroencephalography changes that occur during the transition from EC to the EO are related to the early phase of sensory processing and are defined as activation. In the present study, this process, which is related to bottom-up sensory processing, was examined for the first time. The findings indicate that cognitive impairments in SH begin in the initial phase of sensory processing.*

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ABSTRACT

Objective: Electroencephalography changes that occur during the transition from eyes-closed to the eyes-open state in resting condition are related to the early phase of sensory processing and are defined as activation. The present study aimed to reveal the potential deteriorations that may occur in the initial period of sensory processing in resting electroencephalography between children with subclinical hypothyroidism and a control group.

Materials and Methods: Electroencephalographies of 15 children with subclinical hypothyroidism and 15 healthy children aged 10 to 17 years were recorded for 2 minutes for EC and 2 minutes for eyes-open conditions in resting state. Absolute electroencephalography band powers (μV^2) within the delta, theta, alpha, and beta frequency bands were calculated in Fz, Cz, Pz, and Oz electrodes, respectively, for eyes-closed and eyes-open conditions.

Results: The results show that, although there was no noteworthy difference between the powers of the electroencephalography frequency bands of children with subclinical hypothyroidism and healthy children during the eyes-open condition, the alpha powers of the control group were significantly higher in all electrodes during the eyes-closed condition. Furthermore, the powers of all frequency bands were observed to decrease in the eyes-open condition in the control group. However, the same net decrease was not observed in the frequency powers of children with subclinical hypothyroidism.

Conclusion: According to the results of this study, children with subclinical hypothyroidism may experience information processing impairments starting in the early stages of sensory processing.

Keywords: Resting EEG, children, subclinical hypothyroidism, EEG frequencies

INTRODUCTION

Thyroid hormones play a key role in the maturation of the brain and normal brain functions throughout life. Many studies show that thyroid dysfunctions lead to cognitive impairments and mood changes.[1-6] Although attenuation of cognitive processes in primary hypothyroidism is a well-defined phenomenon, how cognitive functions are affected in subclinical hypothyroidism (SH) is still controversial.[7-9] In SH, thyroid-stimulating hormone (TSH) levels are slightly elevated, whereas free T4 and T3 are within the normal interval. In a study investigating brain electrical activity by electroencephalography (EEG), It is observed that children with SH show reduced P3 amplitude, which is the brain potential evoked against the stimulus

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to which attention is directed.[10] P3 is defined as a mechanism of attention allocation and immediate memory. Studies evaluating the cognitive functions of children and adolescents with SH widely used neurocognitive function tests and reported that children with SH had poor performance in attention tests.[11,12]

Electroencephalography activity provides important information about cortico-cortical and cortical-subcortical networks of the brain.[13] The electrical brain activity recorded over the scalp is the sum of multiple oscillations at different frequencies. The spectral analysis assesses the power of the separate frequency bands in the EEG. These frequencies from low to high are defined as delta (0.5-3.5 Hz), theta (3.5-7 Hz), alpha (8-14 Hz), beta (15-30 Hz), and gamma (30-48 Hz). Some features (duration, location) of these oscillations and the transition between them are used to characterize the state of the brain, such as alpha, theta, and delta. Frequencies are evaluated in sleep scoring; in wakefulness, the fluctuations in these EEG frequencies reflect arousal level and vigilance.[14] Dysregulations in vigilance may alter higher cognitive functions such as attention, memory, and executive frontal functions.[14]

Studies have shown that various characteristics of the background EEG and power spectrum are quite differentiated in attention-deficit and hyperactivity disorders, schizophrenia, Alzheimer's disease, and bipolar disorder.[15-20] There have been a relatively limited number of electrophysiology studies in hypothyroidism. Slowing of dominant rhythm is typically found in hypothyroidism.[21-23] Pohunková et al[23] showed an increased percentage representation of fast frequencies in the beta band. These data suggest that the thyroid hormones influence the EEG rhythm formation in primary hypothyroidism. As far as we know, there is only 1 study evaluating the resting EEG activity in SH, and it has been shown that alpha activity is decreased in the right hemisphere and bilaterally in the frontal areas in young women affected by SH.[24]

The present study analyzes the resting state brain electrical activity in children with SH. While moving from the eyes-closed (EC) state to eyes-open (EO) state, visual information input starts. Visual input enhanced the functional innervation of the visual system, which activates the entire brain.[15] Electroencephalograph changes that occur during the transition from EC to the EO are related to bottom-up (early phase of) sensory processing and are defined as activation. To date, there are no studies investigating resting EEG rhythms and activation in children with SH. Herein, we aimed to characterize the differences in resting EEG and arousal difference between EO and EC resting conditions between children in SH and control groups.

MATERIALS AND METHODS

Participants

Fifteen children with SH were included in the study. Subclinical hypothyroidism was defined based on elevated serum TSH levels (TSH, 4.94-20 mIU/L) and serum fT4 levels within the normal range.[25] These levels were confirmed with a second measurement 4-6 weeks later. The control group consisted of 15 healthy children. Children with any disease that could affect cognitive processes or who were taking iodine-containing drugs and medications that affected cognition were excluded from both groups. None of the participants had a history of cognitive or psychiatric disorders in first-degree relatives. The children in the study were reported to show normal academic performance at school.

The study was approved by the İzmir Katip Çelebi University Clinical Research Ethics Committee (21.11.2013, approval number: 173). The parents of the children gave written informed consent before participating in the study. The study was carried out in accordance with the principles of the Declaration of Helsinki.

Experimental Procedure

Each subject was seated in a chair in an isolated room. Electroencephalography of the subjects was recorded for 2 minutes for EC and 2 minutes for EO conditions in resting state. Electroencephalography recordings were taken from all participants in the same recording laboratory, in the same posture and with the same recording system, and settings. All recordings were done between 10:00 AM and 04:00 PM. Children who did not consume any caffeine-containing food or drink (e.g., tea, coffee, or chocolate) at least 3 hours before the recording were included. Additionally, the same recording team took the recordings each time.

Electroencephalography was recorded from 30 Ag/AgCl electrodes using a BrainAmp 32-channel system (Brain Products, Munich, Germany). 10/20 Jasper BrainVision EEG caps that were appropriate for the children's head sizes were used. The EEG was amplified through a BrainAmp with band limits of 0.1-250 Hz. Two electrodes attached to the earlobes (A1+A2) were used as reference. Impedances were kept below 10 kΩ. Electroencephalography was digitized at a 1000 Hz/s sampling rate with a 0.1-70 Hz bandpass filter. A 50-Hz notch filter was also applied. Electrooculography (EOG) activity was recorded bipolar with Ag/AgCl electrodes placed in the outer cantus and infraorbital area in the right eye.

Data Analysis

Subsequent analyses were performed separately for EC and EO resting EEG data. Electroencephalography data were analyzed using a BrainVision Analyser (Brain Products) and filtered offline with a band-pass filter between 0.1 and 48 Hz. The data were fragmented offline in consecutive epochs of 1 second. Eye movement or artifact-containing epochs were manually rejected offline. The digital Fast Fourier Transform (FFT)-based power spectrum analysis was performed using a 10% Hamming window to obtain the results in the absolute EEG band power (μV^2) at each electrode within the following bands: delta (0.5-3.5 Hz), theta (3.5-7.5 Hz), alpha (7.5-12.5 Hz), and beta (12.5-30 Hz). These power values were averaged across the epochs of EC and EO conditions. The areas as the raw sum (RS) of band power values were calculated using electrodes Fz, Cz, Pz, and Oz.

Statistics

The Statistical Package for the Social Sciences version 25 software was used for statistical analysis. The distribution characteristics of the variables were examined using the Shapiro–Wilk test. Normally distributed independent data were evaluated using the *t*-test, and nonparametric independent samples were evaluated using the Mann–Whitney *U*-test. Power values of EEG bands in EC and EO conditions were compared using the paired-samples *t*-test and Wilcoxon test for parametric and nonparametric evaluations, respectively. Frequency band power changes due to the transition from EC to EO conditions were evaluated using the following formula:

$$\text{Percentage change of the raw sum of power} = \frac{\text{EO raw sum of power value} - \text{EC raw sum of power value}}{\text{EC raw sum of power value}}$$

(for each frequency band). The percentage change of the RS of power in each frequency band was compared between the SH and control groups.

RESULTS

Participant Demographics

The TSH levels of children with SH ranged between 5.39 and 13.19 mIU/L. The TSH level was significantly higher in children with SH (6.99 ± 2.23 mIU/L) compared with the controls (1.49 ± 0.42 ml/L; t(25) = −5.838; *P* < .001). FT4 levels of SH (16.05 ± 1.92 pmol/L) and the control group (16.10 ± 1.65 pmol/L) were in the normal range and there was no statistical difference between the groups. There were 15 children with SH (age range 10-17 years, mean age = 13.9 ± 3.2 years; 10 females) and 15 healthy children in the study (age range 11-17 years, mean age = 13.6 ± 2.8 years; 11 females). There was no statistical difference between the groups concerning age.

Comparison of Electroencephalography Band Powers Between Children with Subclinical Hypothyroidism and Controls

The areas as the RS of EEG band powers for the children with SH and controls were calculated using Fz, Cz, Pz, and Oz electrodes for EC and EO conditions (Table 1).

In the Eyes-Closed Condition

According to the independent samples *t*-test, the RS of theta band power in the Oz electrode was larger for controls (M = 150.16, SD = 56.05) compared with children with SH (M = 91.10, SD = 60.20; t(28) = −2.54; *P* = .02). The control group RS of alpha band power was larger in the Fz (M = 56.44, SD = 27.66) channel compared with children with SH (M = 32.92, SD = 14.90; t(28) = −2.51; *P* = .02). The control group RS of alpha band power was larger in the Oz (M = 150.16, SD = 56.05) channel compared with children with SH (M = 91.10, SD = 60.20; t(28) = −2.54; *P* = .02) (Figure 1).

The Mann–Whitney *U*-test revealed that the RS of alpha power in the Cz electrode was larger in the control group (Mdn = 79.91; Q1 = 39.35 − Q3 = 95.06) compared with the SH group (Mdn = 40.85; Q1 = 33.77 − Q3 = 64.27), (U = 164; *P* = .03). The RS of alpha band power in the Pz electrode was also larger for controls (Mdn = 107.67; Q1 = 77.24 − Q3 = 145.99) compared with children with SH (Mdn = 64.71, Q1 = 56.45 − Q3 = 82.25) (U = 180; *P* = .005) (Figure 1).

In the Eyes-Open Condition

The Mann–Whitney *U*-test revealed that the RS of theta power in the Oz electrode was larger in children with SH (Mdn = 27.46; Q1 = 17.61 − Q3 = 35.24) compared with the controls (Mdn = 15.03; Q1 = 13.08 − Q3 = 17.30) (U = 40; *P* = .003) (Figure 1).

Table 1. Area as Raw Sum of EEG Band Powers (μV²) (Mean ± Standard Deviation)

	SH		Control	
	EC	EO	EC	EO
Delta				
Fz	55.72 ± 17.89	76.85 ± 33.85	59.57 ± 14.04	58.47 ± 15.55
Cz	54.97 ± 18.13	62.28 ± 22.75	65.49 ± 22.09	60.31 ± 18.49
Pz	66.39 ± 44.28	55.03 ± 14.74	62.96 ± 23.56	52.24 ± 17.82
Oz	42.49 ± 17.32	61.16 ± 40.25	56.33 ± 32.78	44.60 ± 20.95
Theta				
Fz	31.63 ± 20.35	36.01 ± 18.81	34.21 ± 9.14	25.74 ± 9.61
Cz	32.60 ± 19.83	34.99 ± 15.50	37.75 ± 9.26	28.40 ± 11.71
Pz	36.91 ± 22.89	29.78 ± 14.48	42.50 ± 15.28	21.88 ± 8.31
Oz	22.54 ± 12.35	29.48 ± 17.52	33.78 ± 9.91	15.08 ± 3.78
Alpha				
Fz	32.92 ± 14.90	21.62 ± 13.92	56.44 ± 27.66	20.92 ± 11.40
Cz	48.70 ± 31.65	35.04 ± 34.76	80.75 ± 41.02	30.15 ± 20.01
Pz	64.99 ± 22.89	60.08 ± 61.51	136.90 ± 95.09	45.64 ± 37.40
Oz	91.10 ± 60.20	44.69 ± 41.23	150.16 ± 56.05	35.69 ± 19.49
Beta				
Fz	13.03 ± 5.31	13.34 ± 5.91	13.72 ± 4.13	10.95 ± 4.16
Cz	13.07 ± 5.39	12.03 ± 5.73	15.36 ± 4.50	11.28 ± 4.45
Pz	15.96 ± 9.10	13.31 ± 7.05	18.43 ± 5.65	10.79 ± 3.72
Oz	20.06 ± 10.33	14.51 ± 7.48	24.56 ± 12.43	13.27 ± 4.39

EC, eyes-closed condition; EEG, electroencephalography; EO, eyes-open condition; SH, subclinical hypothyroidism.

There were no other significant differences in the RS of EEG band powers between the controls and subjects with SH.

COMPARISON OF ELECTROENCEPHALOGRAPHY BAND POWERS BETWEEN EYES-CLOSED AND EYES-OPEN CONDITIONS

Children with Subclinical Hypothyroidism

The paired-samples *t*-test showed that the RS of delta power in the Fz electrode during the EC condition (M = 55.72, SD = 17.89) was significantly lower than the EO condition (M = 76.85, SD = 33.85; t(14) = −2.415; *P* = .03). The RS of alpha power in the Fz electrode during the EC condition (M = 32.92, SD = 14.90) was significantly higher compared with the EO condition (M = 21.62, SD = 13.92; t(14) = 2.278; *P* = .04). The Wilcoxon signed-rank test indicated a significant difference solely in the RS of alpha power in the Oz electrode under the EC (Mdn = 81.25) and EO conditions (Mdn = 38.94) with a mild effect size (r = 0.62) (z = 2.385; P =.02).

Control Group

The RS of theta, alpha, and beta powers was significantly higher in all channels during the EC condition compared with the EO condition (Figure 2).

According to the paired samples *t*-test, the RS of alpha power during the EC condition in the Fz (M = 56.44, SD = 27.66) electrode was significantly higher compared with EO in the Fz (M = 20.92, SD = 11.40; t(14) = 5.56; *P* = .001).

According to the Wilcoxon signed-rank test, EC condition had higher RS of powers compared to EO condition. Statistically significant reduction in the RS of delta power is found only in

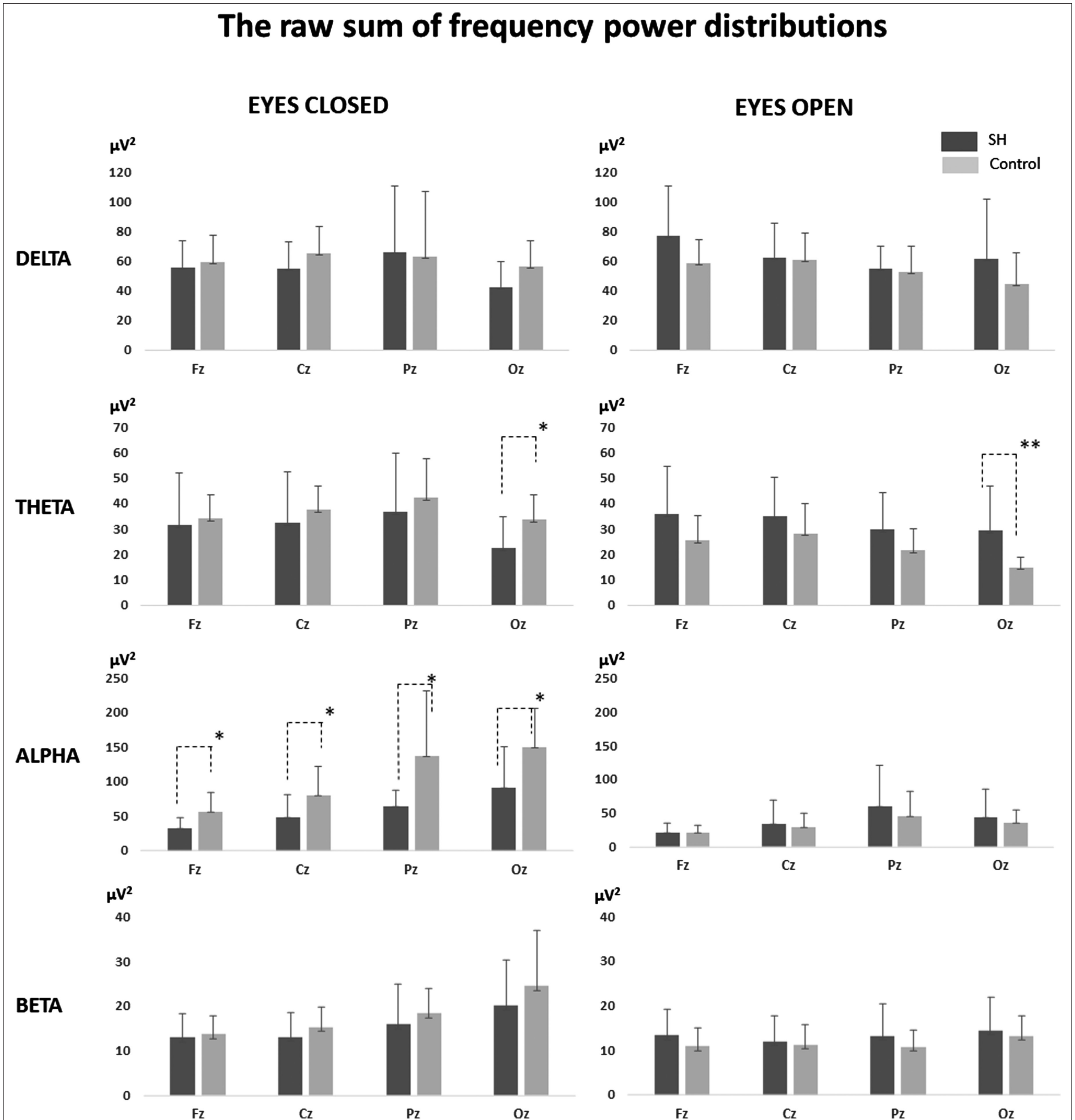

Figure 1. The raw sum of delta, theta, alpha, and beta frequency powers is presented from top to down in µV² units. The dark-colored blocks in the graph represent the neuroelectric activity of children with subclinical hypothyroidism, and light-colored blocks depict the activity of the control group. The dashed lines above the columns show the statistical significance of the difference between the 2 values. Error bars show standard deviation. $*P < .05$ and $**P < .005$.

Pz electrode. Delta power in EC condition (Mdn = 60.78) was significantly higher than EO condition (Mdn = 53.61; $z = -2.05$; $P = .04$) with a low effect size ($r = .53$).

In terms of theta and beta powers, EC condition had significantly higher values compared to EO condition in all electrode sites. The RS of theta power in Fz electrode in EC condition (Mdn = 32.83) was higher than that of EO condition (Mdn = 26.37; $z = -2.61$; $P = .009$; $r = .67$). The RS of theta power in Cz in EC (Mdn = 37.18) was higher than EO (Mdn = 25.61; $z = -2.67$; $P = 0.008$ and $r = 0.69$). The RS of theta power in Pz was greater in EC (Mdn = 41.18) than in EO (Mdn = 20.31; $z = -3.35$; $P = .001$) with a large effect size ($r = .86$). The Oz RS of theta power was larger in the EC condition (Mdn = 33.41) than in the EO condition (Mdn = 15.03; $z = -3.35$; $P = .001$), indicating yet another significant effect size ($r = .86$). The RS of

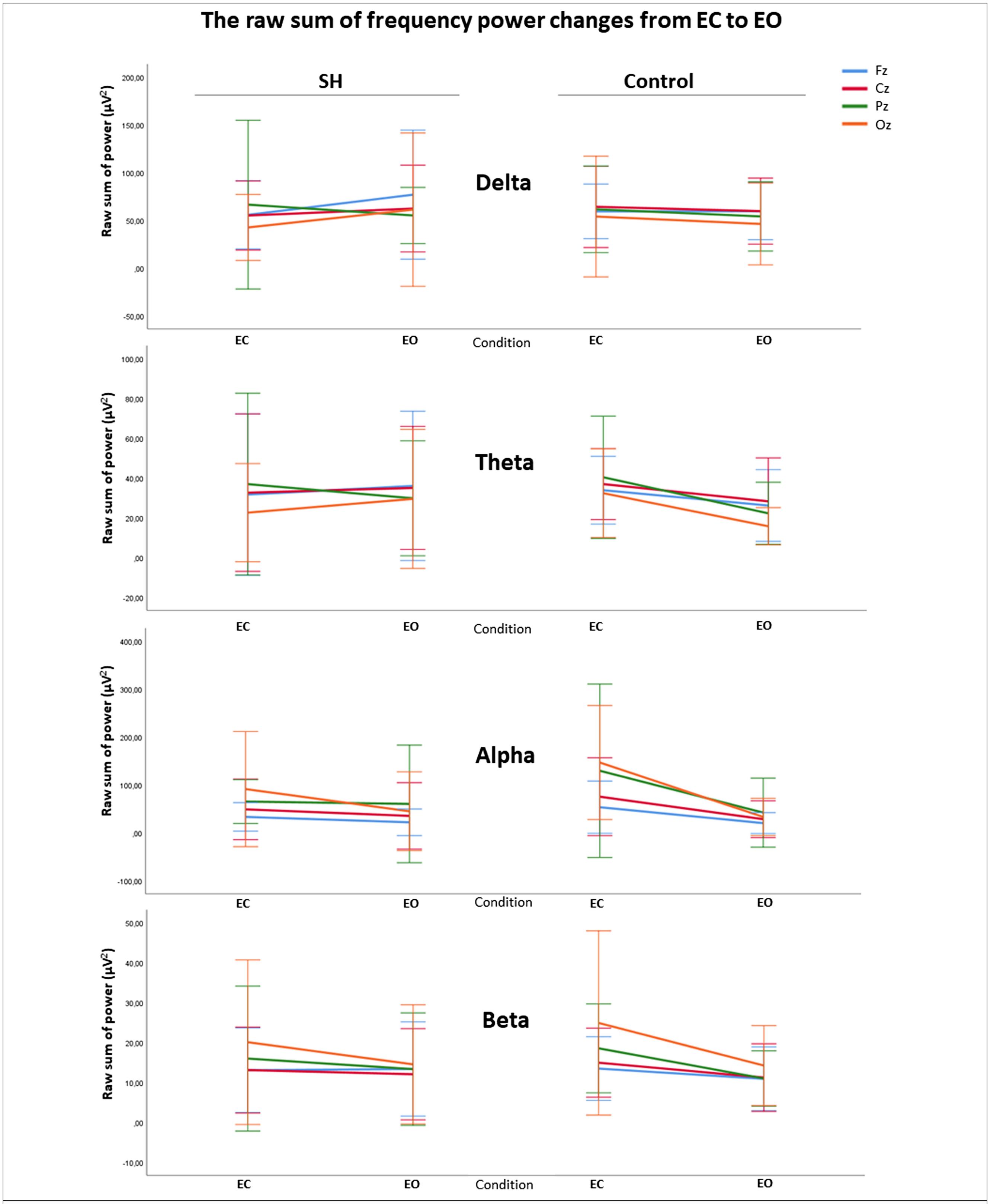

Figure 2. The change of raw sum of delta, theta, alpha, and beta frequency powers from the eyes-closed condition to the eyes-open is presented in μV² units. The control group is shown on the left and the subclinical hypothyroidism group is shown on the right in each of the frequency graphs. Error bars show standard deviation. EC, eyes closed; EO, eyes open.

beta power was larger in EC (Mdn = 33.27) compared with EO (Mdn = 26.37; z = −3.18; *P* = .001) in Fz site with a high effect size (r = .82). Again with a strong effect size (r = .91), the RS beta power in Cz was higher in the EC condition (Mdn = 14.11) than in the EO condition (Mdn = 10.79; z =−3.51; *P* = .001). The RS of beta power was larger in Pz electrode in EC (Mdn = 16.22) compared with EO (Mdn = 10.69; z = −3.41; *P* = .001, and r = 0.88). The RS of beta power was larger in Pz electrode in EC (Mdn = 16.22) compared with EO (Mdn = 10.69; z = −3.41; *P* = .001 and r = 0.88). In Oz electrode, compared to the EO condition (Mdn = 14.37), the RS beta power was greater in the EC condition (Mdn = 21.12; z = −3.35; *P* = .001 and r = .86).

In terms of alpha powers, EC condition had significantly higher values compared to EO condition in all electrode sites (z = −3.41; *P* = .001) with a strong effect size (r = .88). The RS of alpha power in Cz electrode in EC (Mdn = 80.11) reduced in EO (Mdn = 23.99). The RS of alpha power in Pz electrode in EC condition (Mdn = 116.26) was higher than that of EO condition (Mdn = 35.92). In Oz electrode, compared to the EO condition (Mdn = 31.63), the RS alpha power was larger in the EC condition (Mdn = 140.65)

Comparison of Percentage Changes of the Raw Sum of Elect roencephalography Band Powers Between the Subjects Subclinical Hypothyroidism and Control

According to the independent samples *t*-test, the RS of Fz delta power percentage change in children with SH (M = 0.50, SD = 0.71) was found to be higher than that of the control group (M = 0.04, SD = 0.32; t(19.40) = 2.29; *P* = .03). The RS of Fz beta power percentage change in children with SH (M = 0.16, SD = 0.56) was found to be higher than that of the control group (M = −0.2, SD = 0.14; t(15.65) = 2.44; *P* = .03). The RS of Cz theta power percentage change in children with SH (M = 0.46, SD = 0.96) was found to be higher than that of the control group (M = −0.22, SD = 0.26; t(16.06) = 2.66; *P* = .02). The RS of Pz theta power percentage change in children with SH (M = 0.076, SD = 0.69) was found to be higher than that of the control group (−0.41, SD = 0.20; t(16.40) = 2.65; *P* = .02). (Figure 3).

Mann–Whitney *U*-tests revealed that the RS of Fz theta power percentage change was larger in children with SH compared with the controls (U = 60.0; *P* = .03); the RS of Pz alpha power percentage change was larger in children with SH (Mdn = −0.67) compared with the controls (Mdn = −0.42) (U = 42.0; *P* = .003); the RS of Oz theta power percentage change was larger in children with SH (Mdn = −0.77) compared with the controls (Mdn =−0.45) (U = 28.0; *P* = .001); the RS of Oz alpha power percentage change was larger in children with SH (Mdn = −0.77) compared with the controls (Mdn =−0.45) (U = 53.0; *P* = .01) (Figure 3).

DISCUSSION

The findings of alpha response differences between the control and children with SH are striking (Figure 1). In both groups, it is observed that alpha responses are weakened (desynchronized) by opening the eyes. Alpha desynchronization is known to reflect the activation of the entire cortex in response to visual stimulation.[26,27] Statistically significant alpha desynchronization was observed in all electrodes in the control group, and significant alpha attenuation was found only in the Fz and Oz channels in the SH group by opening the eyes (Figure 2). While the alpha responses in the EO condition were very similar in both groups, it is noteworthy that the alpha powers of the control group were higher in all electrodes in the EC condition (Figures 1 and 2). These results indicated a reduction in alpha activity in the EC condition within a group of children with SH compared with healthy children. The present study is the first to report the

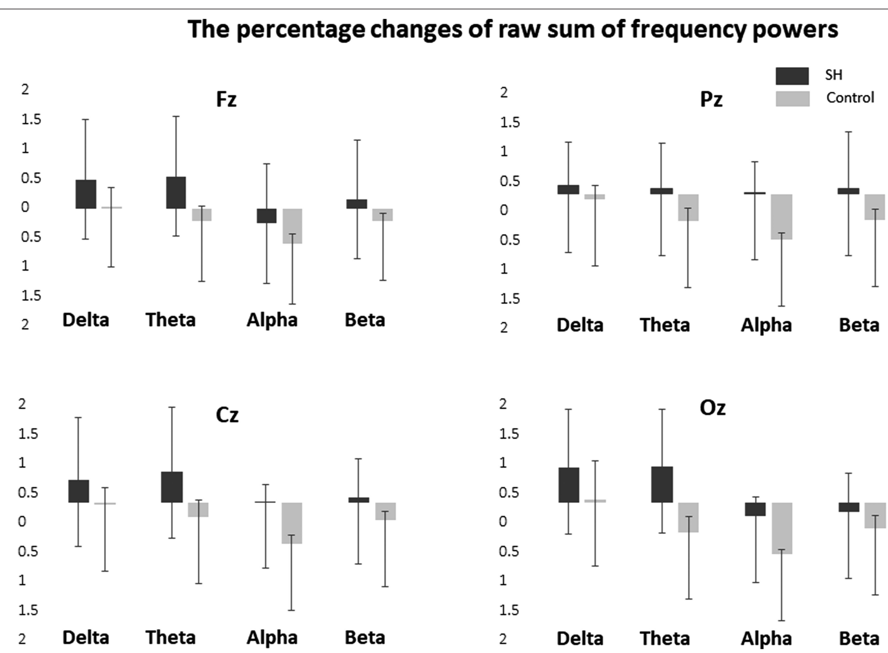

Figure 3. The percentage change of raw sum of delta, theta, alpha, and beta frequencies is presented in Fz, Cz, Pz, and Oz channels, respectively. The dark-colored blocks in the graph represent the percentage change of children with subclinical hypothyroidism, and light-colored blocks depict the percentage change of control group. Error bars show standard deviation.

decrease of alpha activity in children with SH. Menicucci et al[24] observed a reduction of alpha activity in the resting state in young females with SH compared with controls while their eyes were closed. The alpha frequency range dominates occipital electroencephalography activity in adults,[28,29] and alpha power is positively related to cognitive performance and brain maturity[26,30] and plays an important role in controlling attention[31-33] and working memory.[34]

Another remarkable result of the present study is that in the control group, theta, alpha, and beta frequency bands are statistically decreased in almost all channels during the transition from the EC to the EO condition. However, a significant decrease was found only in the Fz alpha and Oz alpha powers in children with SH in the EO condition. In the control group, a significant weakening in the delta power in the Fz site and a significant weakening of the theta, alpha, and beta power in the Fz, Cz, Pz, and Oz sites, respectively, were found during the EC resting state. These findings indicate that there are also differences between children with SH and controls in other frequency bands (theta and beta) powers apart from alpha.

These power differences between the EO and EC conditions become more apparent when the percentage changes in the power of the frequency bands between the 2 groups are compared (Figure 3). Barry et al[35] stated that the EO condition, relative to EC, reflected a state of higher arousal and recommended the EC condition as a baseline standard of arousal and the EO condition as a baseline standard of activation. The increase in the arousal level is an indication of activation because the sensory input increases when the eyes are open.[36] The difference in arousal levels between the EO and EC states is defined as activation.[36] Activation has been shown to contribute to executive functions in children[37] and the most prominent EEG marker of activation in children is a reduction in alpha power in the entire head, along with delta weakening in the frontal and lateral regions, and theta and beta weakening in the posterior regions in the resting state during the EO condition.[38]

In Figure 2, the changes in the power of the frequency bands are seen during the transition from the EC condition to EO. When the control group data are examined, consistent with Barry et al.[38] it is seen that the power of all frequency bands decreases in the EO condition (Figures 2 and 3). However, the same net decrease in frequency powers cannot be observed in children with SH. Even the power values with large standard deviations in this group seem to increase in the EO condition in some electrodes, albeit not statistically significant (Figure 3). This variant frequency power pattern in children with SH may be due to the broad age range of children included in the study. Johnstone et al[39] found that children aged 9-10 years and children aged 11-12 years showed developmental differences in frontal delta, theta, and alpha frequency powers as they transitioned from EC to EO. They reported that although there was a greater decrease in the frontal delta and theta powers in the 9-10 years age group, the decrease was smaller in the 11-12 years age group. In our study, the age range of children with SH was 10-17 years. This wide age range may be the reason for the ambiguity in the power changes during the transition from EC to EO and large standard deviations in the data. However, although there were children in a similar age range (11-17 years; mean age = 13.6 ± 2.8; 11 females) in the control group and there was no statistically significant difference in age, the attenuation of the frequency powers in the EO condition is more stable and evident. Possible neurodevelopmental impairments in children with SH may underlie these power differences between the two groups.

Forgetfulness, lack of attention, and slow information processing are some of the most prevalent cognitive impairments in hypothyroidism. Only a small number of research have examined cognitive abilities in children and adolescents with SH. Due to potential negative effects on the central nervous system, SH in childhood is particularly important and requires additional research. Cognitive batteries are used to assess patients' neuropsychological and behavioral traits in the majority of research examining the effects of SH on cognitive processes. These tests are frequently made to reveal significant cognitive process deficits. Therefore, they might not be able to show the minor thyroid disease-related impairments. Therefore, more reliable techniques that produce objective evidence are needed. To measure brain electrical activity, EEG activity is a reliable, reproducible, and sensitive technique. Electroencephalography activity gives valuable findings about the minute brain changes before behavioral and cognitive symptoms manifest. As a result, the study's results are significant since they point to processing impairments in the early phases of sensory information in SH.

CONCLUSION

Information on the cognitive effects of SH is limited. It has been shown that there are changes in the neuroelectric responses of children with SH compared with healthy children.[10,40] In the present study, it is seen that the activation processes, reflected particularly by the theta, alpha, and beta frequencies of the resting EEG, are different in children with SH and healthy children. These findings suggest that deterioration may begin at a very early level of information processing, through bottom-up processes, in children with SH.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of İzmir Katip Çelebi University (Approval No: 173, Date: 21.11.2013).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – S.K.A., N.O.D., U.E., N.E.E., O.B., M.C.K., B.N.D.; Design – S.K.A., N.O.D., U.E., N.E.E., G.Ç., B.N.D.; Supervision – S.K.A., N.O.D., G.Ç., B.N.D.; Funding – S.K.A., N.O.D.; Materials – S.K.A., N.O.D., U.E., N.E.E., O.B., M.C.K., P.G.; Data Collection and/or Processing – S.K.A., U.E., N.E.E., O.B., M.C.K., G.Ç., P.G., B.N.D.; Analysis and/or Interpretation – S.K.A., N.O.D., U.E.; Literature Review – S.K.A., N.O.D.; Writing – S.K.A., N.E.E.; Critical Review – S.K.A., N.O.D., U.E., O.B., M.C.K., G.Ç., B.N.D.

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